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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 10/594,373 | 09/27/2006 | **Alan Meehan** | 21438P | 1828 |

210 7590 12/15/2009

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| EXAMINER | |
|---|---|
| RAMACHANDRAN, UMAMAHESWARI | |
| ART UNIT | PAPER NUMBER |
| 1627 | |
| MAIL DATE | DELIVERY MODE |
| 12/15/2009 | PAPER |

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/594,373 | MEEHAN, ALAN | |
| | Examiner | Art Unit | |
| | UMAMAHESWARI RAMACHANDRAN | 1627 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *26 August 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-11* is/are pending in the application.

4a) Of the above claim(s) *7-9* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6, 10, 11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *12/11/2006, 6/25/2008,8/26/2009*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

Applicants' election of group I, claims 1-9 and election of finasteride (species for the compounds), metabolic syndrome (disorder) and testosterone (second agent) without traverse in the reply filed on 8/26/2009 is acknowledged. Thus the restriction requirement elected is made final Claims 1, 10, 11 have been amended. Claims 10 and 11 have been amended to read on claim 1. Applicants' have elected finasteride, claims 7-9 are withdrawn from consideration because the claims read on the non-elected species. Accordingly, claims 1-6, 10, 11 will be examined on the merits herein.

### *Application Priority*

This application is a U.S. National Phase application under 35 U.S.C. §371 of PCT Application No. PCT/US2005/010627, filed March 29, 2005, which claims priority under 35 U.S.C. §119 from U.S. provisional application No. 60/558,866, filed April 2, 2004.

### *Information Disclosure Statement*

The information disclosure statements (IDS) filed on 12/11/2008, 6/25/2008, 8/26/2009 is in compliance with the provisions of 37 CFR 1.97. Accordingly, the IDS is being considered by the Examiner.

### *Claim Rejections - 35 USC § 112*

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-6, 10, 11 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for co-administration of 25 mg 3-oxo-4-aza-7.beta.-methyl-16.beta.-(4-methylphenoxy)-5.alpha.-androst-1- ene and 5 mg 17.beta.-(N-tert-butylcarbamoyl)-3-oxo-4-aza-5.alpha-androst-1-en-3-one (finasteride) (Example 4 in specification), N-(2,5-bis-trifluoromethyl-phenyl)-3-oxo-4-aza-4-methyl-5 alpha-androst- 1-ene-17 beta-carboxamide (dutasteride) (Example 5 in specification), N-(2-trifluoromethyl-phenyl)-3-oxo-4-aza-4-methyl-5 alpha-androst-1-ene- 17.beta-carboxamide (Example 6 in specification), 25 mg 3-oxo-4-aza-7.beta.-methyl-16.beta.-(4-methylphenoxy)-5.alpha.-androst-1- ene (Example 7 in specification) in treating abdominal obesity does not reasonably provide enablement for all the compounds encompassed by structural formula I, III and IV (claim 1) in a method of treating visceral adiposity and metabolic syndrome. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The instant specification fails to provide information that would allow the skilled artisan to practice the instant invention without undue experimentation. Attention is directed to *In re Wands*, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors: (1) the nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the ad; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7)

the presence or absence of working examples; and (8) the quantity of experimentation necessary.

***(1)/(2) The Nature of the Invention and Breadth of the Claims:***

The rejected claims are drawn to a method of treating visceral adiposity and metabolic syndrome comprising administering compounds of formula I, III and IV as claimed in claim 1 of the instant application. The claims are very broad with respect to the compounds claimed for the treatment and also with respect to testosterone analogs, precursors, prodrugs etc. Even a cursory calculation of the number of compounds embraced in claim 1 would result in hundreds of compounds.

***(3)/(4) Guidance of the Specification and Working Examples***

The specification provides guidance and working examples related to preparation of Human Prostatic and Scalp 5.alpha.-Reductases, 5.alpha.-Reductase Assay, inhibition Studies of the reductase enzyme, treatment with immunosuppressant cholesterol lowering agents in patients with coronary heart disease (CED) and/or atherosclerotic disease, administration of finasteride in combination with 3-oxo-4-aza-7.beta.-methyl-16.beta.-(4-methylphenoxy)-5.alpha.-androst-1- ene (Example 4 in specification), N-(2,5-bis-trifluoromethyl-phenyl)-3-oxo-4-aza-4-methyl-5 alpha-androst-1-ene-17 beta-carboxamide (dutasteride) (Example 5 in specification), N-(2-trifluoromethyl-phenyl)-3-oxo-4-aza-4-methyl-5 alpha-androst-1-ene- 17.beta-carboxamide (Example 6 in specification), 25 mg 3-oxo-4-aza-7.beta.-methyl-16.beta.-(4-methylphenoxy)-5.alpha.-androst-1- ene (Example 7 in specification) in treating abdominal obesity. The specification in para 008 states that U.S. Pat. Nos. 5,719,158;

5,739,137; 5,910,497; and 6,001,844 and WO 97/10217 and WO 99/22728 disclose additional 5alpha-reductase inhibitors. The specification does not teach or show any combination therapy of any of the compounds with testosterone or testosterone analog or prodrugs. The specification does not show at what dosages of these compounds in combination with testosterone can be effective in treating the conditions claimed.

***(5)/(6) State of the Art and Predictability of the Art:***

Roehrborn et al. has reported on the effects of finasteride on serum T and body mass index in men with BPH (Urology 62(5): 894-899 (2003)) and has presented a poster demonstrating that men with low to low-normal baseline T levels (<400 ng/dL) administered dutasteride demonstrated a larger T increase than men with higher baseline T levels (400 ng/dL) (European Urology 2002; Supplements vol. 1, No., 107). Bhasin in Clinical Infectious Diseases, 2003, 37, S142-S149 teaches that testosterone administration to middle aged men is associated with decreased visceral fat and glucose concentrations and increased insulin sensitivity (see abstract). Amory in The Journal of Clinical Endocrinology & Metabolism, 2004, 89(2), 503-10, reports that exogenous testosterone or testosterone with finasteride increases bone mineral density in older men with low serum testosterone. Marin et al. (Obesity Research, 1, 4, July 1993, 245) reports that from the experimental results they obtained in administration of testosterone that it is suggested that supplementation of abdominal obese men with moderate doses of T might have several beneficial effects. Boyanov et al. (The Aging Male, 2003, 6, 1-7) teaches testosterone supplementation in men with type 2 diabetes, visceral obesity and partial androgen deficiency induces therapeutic benefits. Rebuffe-

Scrive (Int J of Obesity, 1999, 15, 791-95) teaches the effects of testosterone on abdominal adipose tissue in men. Pitteloud et al in Diabetes Care, 28, 1636-1642, 2005 that low serum testosterone levels are associated with an adverse metabolic profile and suggest a novel unifying mechanism for the previously independent observations that low testosterone levels and impaired mitochondrial function promote insulin resistance in men. Amory in The J of Clinical Endocrinology & Metabolism, 90, 5, 2610-17 reports a pharmacokinetic study of oral testosterone in oil plus dutasteride in Men and states that the combination resulted in unexpected and potentially therapeutic increases in serum testosterone. Roehrborn et al. (Urology, 62, 2003, p 894-899) teaches the effects of finasteride on serum testosterone and body mass index in men with benign prostatic hyperplasia. The reference teaches that finasteride, a selective inhibitor of type II alpha reductase, and decreases the conversion of endogenous testosterone to dihydrosterone (DHT) (see Abstract, introduction, para 1). Also, the reference reports that the larger testosterone increases seen in finasteride-treated patients in the lower baseline testosterone tertiles ranging from 0.6-0.8 $kg/m^2$.The main components of the metabolic syndrome are visceral obesity, glucose intolerance, raised blood pressure and dyslipidaemia (elevated triglycerides, low levels of high-density lipoprotein cholesterol),and a pro-inflammatory and thrombogenic state (Saad et al, The role of testosterone in the metabolic syndrome: a review, J Steroid Biochem Mol Biol. 2009 Mar;114(1-2):40-3). The prior art widely teaches the therapeutic benefits of testosterone with decreased visceral fat and glucose concentrations and increased insulin sensitivity. However, it cannot be predicted from such prior art that every single class of

compound(s) claimed will be useful in treating visceral adiposity or metabolic syndrome disorder in combination with testosterone, testosterone analog, or precursors. The instant method claims a multitude of compounds in treating visceral adiposity or metabolic syndrome disorder. The compounds of structural formula (I), (III) and (IV) are different chemical compounds with different structures, chemical and physical properties, bioavailabilities, pharmacokinetic profiles, and pharmacological efficacy. The compounds with different structures impart highly diverse physical and chemical properties, receptor affinities and treatment efficacies. It is also difficult to predict from the prior art and from the specification the effective dosage amounts of the compounds listed that can be combined with testosterone or testosterone analog, or precursors or prodrugs that will be therapeutically effective combination at all dosage amounts. Also, if patient have other disease states or disease conditions and are undergoing therapy, adverse interactions with other drugs may contraindicate the use of these compounds

***(7) The relative skill of those in the art:***

The relative skill of those in the pharmaceutical development and medical treatment arts is high, requiring advanced education and training.

***(8) The Quantity of Experimentation Necessary:***

In order to enable the instantly claimed methods that commensurate with the entire scope, a large quantity of experimentation would be necessary. With Applicants' guidance provided in the specification and what is known in the prior art the person of ordinary skill in the art would have to conduct experiments testing the compounds claimed to find whether each compound of formula (I), (III), (IV) is useful in treating

visceral adiposity and metabolic syndrome. In addition, experiments need to be done to find an effective combination therapy of such compounds with testosterone, testosterone analogs, precursors, prodrugs etc. Furthermore a person of ordinary skill in the art has to conduct experiments to find the right dosage amounts of each agent to be a therapeutically effective combination. In order to practice the above claimed invention, one of ordinary skill in the art would have to first envision formulation, dosage, duration, route and an appropriate animal model system to test the composition in a method of treatment of visceral adiposity, metabolic syndrome etc. If unsuccessful, one of ordinary skill in the art would have to envision a modification in the formulation, dosage, duration, route of administration etc. and appropriate animal model system, or envision an entirely new combination of the above and test the system again. The main components of the metabolic syndrome are visceral obesity, glucose intolerance, raised blood pressure and dyslipidaemia (elevated triglycerides, low levels of high-density lipoprotein cholesterol), and a pro-inflammatory and thrombogenic state. Accordingly, one having ordinary skill in the art have to test the compounds in treating all the components of metabolic syndrome and in addition with a second agent (testosterone, testosterone prodrug, precursor etc) in combination therapy. Therefore, it would require undue, unpredictable experimentation to practice the claimed invention of a method of treating metabolic syndrome with the multitude of compounds with different structures listed in claim 1. Genetech, 108 F.3d at 1366 states that “a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion” and “patent

protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable".

***Claim Rejections-35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 10, 11 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for co-administration of 25 mg 3-oxo-4-aza-7.beta.-methyl-16.beta.-(4-methylphenoxy)-5.alpha.-androst-1- ene and 5 mg 17.beta.-(N-tert-butylcarbamoyl)-3-oxo-4-aza-5.alpha-androst-1-en-3-one (finasteride) (Example 4 in specification), N-(2,5-bis-trifluoromethyl-phenyl)-3-oxo-4-aza-4-methyl-5 alpha-androst-1-ene-17 beta-carboxamide (dutasteride) (Example 5 in specification), N-(2-trifluoromethyl-phenyl)-3-oxo-4-aza-4-methyl-5 alpha-androst-1-ene- 17.beta-carboxamide (Example 6 in specification), 25 mg 3-oxo-4-aza-7.beta.-methyl-16.beta.-(4-methylphenoxy)-5.alpha.-androst-1- ene (Example 7 in specification) in treating abdominal obesity and the prior art being enabling for administration of testosterone to middle-aged men and reporting the associated effects that include decreased visceral fat and glucose concentrations and increased insulin sensitivity does not reasonably provide enablement for treating metabolic syndrome with all the pro-drugs of testosterone as claimed. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims. See M.P.E.P. 2164.08. The reference of

Meyer, J, Pharmacokinetics and Biopharmaceutics, 24, pp. 449-459, is used in this rejection.

The factors to be considered in determining whether a disclosure meets the enablement requirements of 35 U.S.C. 112, first paragraph, have been described in In re Wands, 858 F.2d 731,8 USPQ2d 1400 (Fed. Cir., 1988). The court in Wands states, "Enablement is not precluded by the necessity for some experimentation, such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue', not 'experimentation'" (Wands, 8 USPQ2sd 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations" (Wands, 8 USPQ2d 1404). Among these factors are: (1) the nature of the invention; (2) the breadth of the claims; (3) the state of the prior art; (4) the predictability or unpredictability of the art; (5) the relative skill of those in the art; (6) the amount of direction or guidance presented; (7)the presence or absence of working examples; and (8) the quantity of experimentation necessary

While all of these factors are considered, a sufficient amount for a prima facie case is discussed below.

***(1)/(2) The Nature of the Invention and Breadth of the Claims:***

The rejected claims are drawn to a method of treating visceral adiposity and metabolic syndrome comprising administering compounds of formula I, III and IV as

claimed in claim 1 of the instant application. The claims are very broad with respect to the compounds claimed for the treatment and also with respect to testosterone analogs, precursors, prodrugs etc.

***(3)/(4) Guidance of the Specification and Working Examples***

The specification provides guidance and working examples related to preparation of Human Prostatic and Scalp 5.alpha.-Reductases, 5.alpha.-Reductase Assay, inhibition Studies of the reductase enzyme, treatment with immunosuppressant cholesterol lowering agents in patients with coronary heart disease (CED) and/or atherosclerotic disease, administration of finasteride in combination with 3-oxo-4-aza-7.beta.-methyl-16.beta.-(4-methylphenoxy)-5.alpha.-androst-1- ene (Example 4 in specification), N-(2,5-bis-trifluoromethyl-phenyl)-3-oxo-4-aza-4-methyl-5 alpha-androst-1-ene-17 beta-carboxamide (dutasteride) (Example 5 in specification), N-(2-trifluoromethyl-phenyl)-3-oxo-4-aza-4-methyl-5 alpha-androst-1-ene- 17.beta-carboxamide (Example 6 in specification), 25 mg 3-oxo-4-aza-7.beta.-methyl-16.beta.-(4-methylphenoxy)-5.alpha.-androst-1- ene (Example 7 in specification) in treating abdominal obesity. The specification in para 008 states that U.S. Pat. Nos. 5,719,158; 5,739,137; 5,910,497; and 6,001,844 and WO 97/10217 and WO 99/22728 disclose additional 5alpha-reductase inhibitors. The specification does not teach or show any combination therapy of any of the compounds with testosterone or testosterone analog or prodrugs. The specification does not show at what dosages of these compounds in combination with testosterone can be effective in treating the conditions claimed. The specification is not adequately enabled to show how to make prodrugs of testosterone

or using prodrugs of testosterone along with the compounds claimed in claim 1 in treating metabolic syndrome disorder.

***(5)/(6) State of the Art and Predictability of the Art:***

The state of the art and the predictability of the art as stated above in the 112(1) enablement rejection. The state of the prodrug art is summarized by Wolff, Manfred E., Burger's Medicinal Chemistry and Drug Discovery, Fifth Ed., Vol. 1: Principles and Practice, John Wiley & Sons, 1995,975. The table on the left side of page 976 outlines the research program to be undertaken to find a prodrug. The Second paragraph in section 10 and the paragraph spanning pages 976-977 indicate the low expectation of success. In that paragraph the difficulties of extrapolating between species are further developed. Since the prodrug concept is a pharmacokinetic issue, the lack of any standard pharmacokinetic protocol discussed in the last sentence of this paragraph is particularly relevant. Banker, Gilbert S. et al., Modem Pharmaceutics, Marcel Dekker, New York, 1996, in the first sentence, third paragraph on page 596 states that "extensive development must be undertaken" to find a prodrug. It is well-established that "the scope of enablement varies inversely to the degree of unpredictability of the factors involved", "and physiological activity is generally considered to be an unpredictable factor." In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). Finding a prodrug is an empirical exercise. Predicting if a certain ester of a claimed alcohol, for example, is in fact a prodrug, and produces the active compound metabolically, in man, at a therapeutic concentration and at a useful rate, is filled with experimental uncertainty. Although attempts have been made to predict drug

metabolism de novo, this is still an experimental science. For a compound to be a prodrug, it must meet three tests. First, the prodrug must itself be biologically inactive. Second, the prodrug must be metabolized to a second substance in a human at a rate and to an extent to produce that second substance at a physiologically meaningful concentration. Thirdly, that second substance must be biologically active.

*(7) The relative skill of those in the art:*

The relative skill of those in the pharmaceutical development and medical treatment arts is high, requiring advanced education and training.

***(8) The Quantity of Experimentation Necessary:***

Considering the state of the art as discussed by the references above, and the high unpredictability in the art as evidenced therein, and the lack of guidance provided in the specification, one of ordinary skill in the art would be burdened with undue experimentation to practice the invention commensurate in the scope of the claims. Not all prodrugs of testosterone would be expected to be as effective as testosterone itself. As such, one of ordinary skill in the art would be burdened with undue experimentation to determine specifically which prodrug would be effective and safe for treating metabolic syndrome disorder. Substantial and undue experimentation would be needed to practice Applicant's invention because the specification lacks sufficient detail to show how to make and use the prodrugs of testosterone in treating metabolic syndrome disorder. In view of the above factors one having ordinary skill in the art would have to undergo an undue amount of experimentation to make the instantly claimed invention commensurate in scope with the claims

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-6, 10-11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Roehrborn et al. (Urology, 62, 2003, p 894-899) and McConnell et al. (Applicants' cited IDS: J of Clin Endocrinology and Metabolism, 74, 3, 1992, 505-508) in view of Bhasin et al. (Applicants' cited IDS: Clinical Infectious Diseases, 2003, 37, S142-S149) and Boyanov et al. (Applicants' cited IDS: The Aging Male, 2003, 6, 1-7).

Roehrborn et al. teaches the effects of finasteride on serum testosterone and body mass index in men with benign prostatic hyperplasia. The reference teaches that finasteride, a selective inhibitor of type II alpha reductase, increases the serum testosterone level and decreases the conversion of endogenous testosterone to dihydrosterone (DHT) (see Abstract, introduction, para 1). Also, the reference reports that the larger testosterone increase is seen in finasteride-treated patients in the lower

baseline testosterone tertiles ranging from 0.6-0.8 kg/$m^2$. It is well known that bbody mass index (BMI) is the most widely used measure to diagnose obesity. The reference teaches administration of finasteride to patients with serum testosterone level of <=330 ng/dL (table 1).

McConnell et al. teaches finasteride, an inhibitor of 5-alpha reductase suppresses prostatic dihydrotestosterone in men and increase in testosterone concentration (see abstract, fig.1, 2). The reference teaches decrease in concentration of dihydrotestosterone to 1.14+/-0.3 nmol/kg after finasteride administration and the placebo group had a mean dihydrotestosterone level of 10.3+/-0.6 nmol/kg. The results teaches a reduction of about 30% or more upon administration of finasteride.

The references do not teach the compounds to be useful in the treatment of a male subject with metabolic syndrome (elected species).

Bhasin teaches the effects of testosterone administration on fat distribution, insulin sensitivity and atherosclerosis progression (see Abstract). The reference teaches that testosterone administration to middle-aged men is associated with decreased visceral fat and glucose concentrations and increased insulin sensitivity (see Abstract).

Boyanov etal. teaches that supplementation of testosterone in men with type 2 diabetes, visceral obesity and partial androgen deficiency improved several features of the metabolic syndrome, including glucose homeostasis and body composition (decrease in visceral obesity) and improved symptoms of androgen deficiency (see Abstract, p4, Table 1, p 6, col. 2 para 4). Boyanov teaches a reduction in the waist hip ratio of the patients after month 3 (Table 1). The reference in the Results section reports

that waist-hip ratio decreased by 3.96% in the TU-treated group and body fat decreased by 5.6%.

It would have been obvious to one of ordinary skill in the art at the time of the invention to have used 5-alpha reductase inhibitor compound such as finasteride in the treatment of a male subject with metabolic syndrome because of the teachings of Roehrborn, McConnell, Bhasin and Boyanov etal. Roehrban et al. teaches finasteride, an alpha 5- reductase inhibitor increases the serum testosterone level, decreases DHT level and further teaches that finasteride treatment led to significant mean reduction in the body mass index. Bhasin and Boyanov et al. teach the effects and benefits of testosterone administration to male subjects. The references teaches that supplementation of testosterone hormone is beneficial in the treatment of type II diabetes, visceral obesity, metabolic syndrome etc. The 5-alpha reductase inhibitor compounds inhibit the reductase enzyme thus maintaining the levels of testosterone before they bind to the enzyme and get converted to DHT. Accordingly, it would have been obvious to one having ordinary skill in the art to use finasteride in treating metabolic syndrome because the prior art teaches that administration of finasteride increases the amount of testosterone and testosterone administration to middle-aged men is associated with decreased visceral fat and glucose concentrations and increased insulin sensitivity. One having ordinary skilled in the art would have been motivated to use finasteride and add testosterone as a second agent in treating metabolic syndrome in expectation of therapeutic benefits in attaining decreased visceral adiposity, glucose concentrations and increased insulin sensitivity.

The above said references do not teach that the waist circumference of the male subject to be greater than 102 cm.

. It would have been obvious to one of ordinary skilled in the art at the time of the invention to treat male patients with a waist greater than 102 cm with a compound such as finasteride because waist circumference is a common measure used to assess abdominal fat content and is associated with obesity. The prior art teaches administration of finasteride increases serum testosterone and testosterone has been shown to be associated with decreased visceral fat and glucose concentrations and increased insulin sensitivity and the prior art reports the reduction of waist to hip ratio upon administration of testosterone. One having ordinary skill in the art would have been motivated to select a male patient with a waist greater than 102 cm for treating metabolic syndrome administering a compound such as finasteride in order to decrease the abdominal fat.

**Conclusion**

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to UMAMAHESWARI RAMACHANDRAN whose telephone number is (571)272-9926. The examiner can normally be reached on M-F 8:30 AM - 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on 571-272-0629. The fax phone

number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/SREENI PADMANABHAN/
Supervisory Patent Examiner, Art Unit 1627